Assessment of executive functions in elderly stroke patients:

Long-term predictive value on functional disability

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Tiivistelmä – Abstrakt – Abstract

Tavoitteet: Aivoinfarktin seurauksena vaikeudet kognition eri osa-alueilla ovat suhteellisen tavallisia ja ne yleistyvät iän myötä. Erityisesti toiminnanohjaustoimintojen tiedetään vaikuttavan aivoinfarktin jälkeiseen toimintakykyyn. Toiminnanohjauksen kliininen arviointi on kuitenkin haastavaa. Hayling-testi, Kuviosujuvuustehtävä ja Kysymystehtävä eivät ole yleistyneet kliiniseen käyttöön toiminnanohjauksen arvioinnissa ja aiempien niitä koskevien tutkimusten määrä on varsin rajallinen. Tässä tutkimuksessa tutkittiin näiden tehtävien toimivuutta ikääntyneillä aivoinfarktipotilailla kolmen kuukauden kuluttua aivoinfarktista. Suoriutumista näissä vakiintumattomissa tehtävissä verrattiin suoriutumiseen perinteisissä toiminnanohjauksen arviointiin käytetyissä menetelmissä. Lisäksi tutkittiin, ennustaako näissä tehtävissä suoriutuminen ikääntyneiden aivoinfarktipotilaiden toimintakykyä seuranta-aikana.

Menetelmät: 62 aivoinfarktipotilasta ja 39 tervettä henkilöä, iältään 55–85 vuotiaita, tutkittiin laajasti sekä neurologisesti että neuropsykologisesti, kun aivoinfarktista oli kuulunut kolme kuukautta. Toiminnanohjausta arvioitiin Trail Making-testillä, Stroop-testillä, Wisconsinin korttien lajittelutehtävällä, Sanasujuvuustehtävällä sekä Hayling-testillä, Kuviosujuvuustehtävällä ja Kysymystehtävällä. Itsenäistä toimintakykyä arjen perustoiminnoissa tutkittiin modified Rankin Scale -kyselylomakkeella (mRS) ja itsenäistä toimintakykyä monimutkaisemmissa toiminnoissa Instrumental activities of daily living -kyselylomakkeella (IADL). Lisäksi 15 kuukauden seurannan jälkeen toimintakykyä arvioitiin mRS-kyselylomakkeella.

Tulokset ja johtopäätökset: Perinteisten toiminnanohjauksen arviointimenetelmien lisäksi Hayling-testi ja Kysymystehtävä erottelivat aivoinfarktipotilaita terveistä verrokeista. Lisäksi aineistossamme toiminnanohjaus ennusti myöhempää toimintakykyä. Hayling-testi oli johdonmukaisesti yhteydessä mRS- ja IADL-kyselylomakkeilla tutkittuun toimintakykyyn kolmen kuukauden kohdalla ja ennusti mRS- kyselyllä tutkittua toimintakykyä 15 kuukauden seurannassa. Hayling-testi osoittautui pysyvimmäksi arviointimenetelmäksi ikääntyneiden aivoinfarktipotilaiden toimintakyvyn ennustajana. Toiminnanohjauksen tarkka arviointi on haastavaa ja tulevaisuudessa tarvitaan vielä tarkempia ja herkempiä menetelmiä sen mittaamiseen. Tämä tutkimus vahvistaa toiminnanohjauksen arvioinnin tärkeyden, kun halutaan ennustaa tulevaisuuden toimintakykyä.

Avainsanat – Nyckelord – Keywords

Toiminnanohjaus, aivoinfarkti, ikääntyminen, neuropsykologinen tutkimus

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Tiivistelmä – Abstrakt – Abstract

Objective: Cognitive impairment as a consequence of a stroke is common. Advanced age increases the frequency of poststroke cognitive deficits. Particularly executive dysfunction has an important role in poststroke disability. Complex by their nature, however, measuring executive function is difficult. The Hayling test, Design fluency task and Questioning task are some of the less common assessment methods of executive functions, and thus, they are not widely studied. The aim of the present study was to assess the feasibility of these tests in elderly patients three months after ischemic stroke. Performances on these tests were compared to conventional assessment methods of executive functions, and their predictive value on functional disability in follow-up was examined.

Methods: 62 stroke patients and 39 control subjects, aged 55-85, underwent comprehensive neurological and neuropsychological examinations three months after the index stroke. Executive functions were studied with the Trail Making test, Stroop test, Wisconsin card sorting test, Verbal fluency task as well as with the Hayling test, Design fluency task and Questioning task. The modified Rankin Scale (mRS) and the Lawton’s Instrumental activities of daily living -scale (IADL) were used to assess functional abilities at three months, and the mRS after 15 months follow-up.

Results and conclusions: The Hayling test and Questioning task and the four conventional tests of executive functions differentiated stroke patients from healthy controls. Furthermore, the executive functions predicted functional dependence in the elderly stroke patients. The Hayling test was most consistently associated with functional disability as evaluated with mRS and IADL three months after the stroke, and predicted functional disability as evaluated with mRS at 15 months follow-up. Of all executive functions tests, the Hayling test proved to be the most constant predictor of functional abilities in elderly stroke patients. However, there is no golden standard for measuring executive functions, and in the future, more sensitive methods are needed. Nevertheless, the present study confirms the importance of assessing executive functions in clinical populations, when predicting functional disability even in the long-term.

Avainsanat – Nyckelord – Keywords

Executive functions, stroke, aging, neuropsychological examination

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ESIPUHE

Tämä Pro gradu-tutkielma on tehty yhteistyössä Helsingin yliopiston ja Helsingin yliopistollisen keskussairaalan (HYKS) Neurologian klinikan kanssa. Käyttämäni aineisto on osaotos laajasta monitieteisestä Helsinki Stroke Aging Memory (SAM) -tutkimushankkeesta. Projektin johtajana toimi professori Timo Erkinjuntti. SAM -tutkimushankkeen aineisto koostuu 486 perättäisestä 55–85-vuotiaasta aivoinfarktipotilaasta Helsingin yliopistollisessa keskussairaalassa. Tutkimusprojektin tarkoituksena oli saada tietoa ikääntyneiden aivoinfarktipotilaiden tilanteesta kolme kuukautta ja 15 kuukautta sairastumisen jälkeen. Monitieteinen tutkimus sisälsi tutkimuspotilaiden laajan neuropsykologisen, neurologisen, neuroradiologisen, logopedisen ja psykiatrisen tutkimuksen. Tässä Pro gradu-tutkielmassa käyttämäni aineisto koostuu 62 perättäisestä alkuperäisen neuropsykologisen tutkimuksen jälkeen toiminnanohjauksen arviointiin painottuneen jatkotutkimuksen läpikäyneestä aivoinfarktipotilaasta.

Tulin mukaan tutkimushankkeeseen tammikuussa 2014, jolloin sain käyttööni yllämainitun jatkotutkimuksen läpikäyneiden potilaiden ja kontrollihenkilöiden alkuperäiset testipöytäkirjat ja SAM -hankkeen raakadatan. Tutkimustyöni alkoi paperisten toiminnanohjaustehtävien pisteytyksellä ja niiden siirtämisellä sähköiseen muotoon. Minun pisteytykseni lisäksi psykologian tohtori, yliopistonlehtori Maarit Virta ystävällisesti teki rinnakkaisen pisteytyksen tehtäville, jolloin arvioitsijoiden välistä luotettavuutta eri menetelmissä oli mahdollista arvioida.

SAM -tutkimushankkeesta on julkaistu lukuisia vertaisarvioituja asiantuntija-artikkeleita kansainvälisissä julkaisuissa, väitöskirjoja ja opinnäytetöitä useilta eri tieteenaloilta. Tämän Pro gradu-tutkielman tarkoituksena oli tarkastella laajemmin toiminnanohjauksen neuropsykologiseen arviointiin liittyviä kysymyksiä, ja toisaalta nimenomaan aivoinfarktin jälkeisten toiminnanohjaustoimintojen vaikutusta myöhempään toimintakykyyn.

Ohjaajinani Pro gradu-työssäni toimivat dosentti Hanna Jokinen-Salmela Helsingin yliopistollisen keskussairaalan Neurologian klinikasta ja psykologian tohtori, yliopistonlehtori Maarit Virta Helsingin yliopistosta. Haluan kiittää molempia ohjaajiani rakentavasta palautteesta, pitkäjänteisestä yhteistyöstä sekä ymmärryksestä silloin, kun sitä tarvittiin. Lisäksi haluan kiittää HYKS Neurologian klinikan johtavaa neuropsykologia dosentti Marja Hietasta, joka mahdollisti mukaan pääsyni SAM -tutkimusprojektiin ja luovutti tutkimushankkeen aineiston käyttööni.

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Hanna Laakso

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1 INTRODUCTION

Stroke is a loss of brain function as a result of disturbance in the brain blood supply. In Finland, the total number of annual first-ever stroke patients was 10 338 in the year 2007 (Meretoja et al., 2011). Stroke is the third most significant cause of disability worldwide (STAKES, 2007). Cognitive impairment after stroke is relatively common. The frequency of cognitive decline or even dementia among stroke survivors increases with increasing age (Pohjasvaara, Erkinjuntti, Vataja & Kaste, 1997). Depending on study protocol the prevalence of cognitive deficits ranges from below 50 % to 90 % among stroke survivors (Gottesman & Hillis, 2010; Jaillard, Naegele, Trabucco-Miguel, Le-Bas & Hommel, 2009; Nys et al., 2007). These deficits may include impairments in specific cognitive domains (Jokinen et al., 2006; Middleton, et. al, 2014; Nys et al., 2007) or in global cognitive functioning (Ballard et al., 2002; Patel, Coshall, Rudd & Wolfe, 2002). Executive functions are one of the most vulnerable cognitive domains in acute stroke (Gottesman & Hillis, 2010; Zinn, Bosworth, Hoenig & Swartzwelder, 2007). Executive functions are by definition higher cognitive capacities and responsible for combining cognitive functions to goal-oriented complex actions, e.g. planning, sequencing and monitoring of one's behavior (Royall et al., 2002; Eslinger & Chakara, 2004).

National Institute of Health Stroke Scale (NIHSS) (Goldstein, Bertels & Davis, 1989) is a widely used rating scale for clinical evaluation of stroke severity. However, it is shown that even among patients with the lowest scores on NIHSS, cognitive deficits are common (Kauranen et al., 2013a). Furthermore, cognitive impairment has a major impact on independent functional abilities poststroke. Cognitive deficits on stroke survivors are related to poor long-term outcome (Kauranen et al., 2013a; Kauranen et al., 2013b) and even higher morbidity (Oksala et al., 2009; Gottesman & Hillis, 2010). Particularly deficits on executive functions have been found to be independent predictors of poor stroke related outcome (Patel et al., 2002) and poor rehabilitation outcome (Zinn et al., 2007).

Complex by their nature, assessing executive functions is difficult. A few methods have been established for clinical use, but specificity on measuring executive functions is still lacking (e.g. Lezak, Howieson & Loring, 2012, p. 87, 612; Stuss, 2007). In addition, the assessment is complicated by the fact executive functions are needed especially in novel and complex situations and environments. Thus, highly structured clinical examination does not always reveal the underlying deficits (e.g. Zinn et al., 2007; Stuss, 2007).

Stroke is the most common neurological cause of disability and lost life-years (Seshadri & Wolf, 2007). In the future, cerebrovascular diseases are assumed to become more common due to increased life expectancy (Sivenius et al., 2009; Seshadri & Wolf, 2007). Deficits in executive functions are associated with functional disability (e.g. Pohjasvaara, Leskelä & Vataja, 2002). Thus, there is a need for more accurate assessment of executive functions for early interventions and for predicting the long-term outcome.

1.1 Ischemic stroke

The continuous supply of glucose and oxygen along the blood circulation are necessary for brain activity. Thus, blood circulation disturbances in the central nervous system can rapidly result in permanent damage in the brain. Stroke is clinically defined as “an acute neurological dysfunction of vascular origin with sudden (within seconds) or at least rapid (within hours) occurrence of symptoms and signs corresponding to the involvement of the focal areas in the brain” (WHO, 1989). Strokes can be divided according to the nature of lesion: Hemorrhage refers to the rupture of an abnormal artery whereas ischemia is an occlusion of a feeding artery (WHO, 1989). Infarcts are defined as permanent damage of brain tissue caused by ischemia. It is estimated that ischemic strokes accounts for 87 % of all strokes (Go et al., 2013).

According to their etiology ischemic strokes are divided (TOAST-classification; Trial of Org 10172 in Acute Stroke Treatment; Adams et al., 1993) as large artery atherosclerosis (embolus or thrombosis), lacunar infarcts (small vessel occlusion) or cardioembolisms. Stroke can be also defined according to cerebral circulation: Carotid area infarcts can be divided into frontal and middle circulation infarcts, and when the infarct is located in the verterobasillar area, it is called posterior circulation infarct. In a European population based study (Kolominsky-Rabas, Weber, Gefeller, Neundoerfer & Heuschmann, 2001) the prevalence of stroke subtypes was as follows: large artery atherosclerosis 13 %, cardio embolism 27 %, small artery occlusion 23 %, stroke of other determined cause 2 % and stroke of undetermined cause 35 %. In addition, the etiology of an infarct may be conditional to age and sex. Cardiovascular embolisms and small vessels disease are more common causes in the elderly (Telman, Kouperberg, Sprecher & Yarnitsky, 2008), and large artery atherosclerosis and small artery occlusions may have higher incidence among men compared to women (Kolominsky-Rabas et al., 2001).

Risk factors for stroke are well documented. High blood pressure (Lee et al., 2011; Goldstein et al., 2011), smoking, obesity and especially abdominal body fat, excessive alcohol consumption and some medical conditions e.g. metabolic syndrome (Goldstein et al., 2011) are modifiable risk factors and they can be affected with primary prevention. Risk factors such as increased age, gender, or genetic predisposition are generally non-modifiable. Advanced age and male-sex are both important independent risk factors for stroke (e.g. Goldstein et al. 2011).

1.1.1 Poststroke functional impairment

Stroke is related to severe risk of disability (e.g. Adamson, Beswick & Ebrahim, 2004). Consequences of stroke can be multifaceted depending on the stroke severity, location of damaged brain tissue or patients characteristics (Reid et al., 2010; Kelly-Hayes et al., 2003). In a population based study, increasing age was the main contributor to deficits in physical (i.e. motor functions including paresis or speech), cognitive, affective, and social domains after stroke (Kelly-Hayes et al., 2003). Furthermore, poststroke depression is common among stroke patients: In a Finnish hospital based study of stroke patients, depression was diagnosed in 18 % of the stroke patients without other explanatory factors besides stroke, and depression diagnosis was correlated with dependence in daily life (Pohjasvaara et al., 1998a). Thus considering stroke patients' independence in everyday functions, other factors in addition to physical impairments are important (e.g. Pohjasvaara, Vataja, Leppävuori, Kaste & Erkinjuntti, 2001a). Independent functional abilities decrease after stroke relatively more in older than in younger age (Pohjasvaara et al., 2001a), so the elderly are at higher risk to remain dependent. Also, in an American population based study (Dhamoon et al., 2010), stroke patients' declined quality of life was associated with advanced age, mood disturbances, stroke severity, urinary incontinence, functional status, cognition and stroke laterality.

Independent living is an important measure for stroke outcome (Pohjasvaara, Erkinjuntti, Vataja & Kaste, 1998b). American Heart Association has estimated that 25 % to 74 % of stroke survivors worldwide require at least some assistance or are fully dependent in activities of daily living (ADLs) (Miller et al., 2010). Activities of daily living include basic functions for everyday life, i.e., bathing, dressing, toileting, transferring, continence, and feeding. Basic ADL functions after stroke are commonly assessed with different ranking scales e.g. Katz scale (Katz, Ford, Moskwitz, Jackson & Jaffe, 1963), Barthel Index (Mahoney & Barthel, 1965), and modified Rankin Scale (mRS) (Banks & Marotta, 2007; Rankin, 1957). These functional rating scales are based on self-ratings or evaluations by nursing staff or a family member.

Independence in more complex everyday functions is often assessed with Instrumental activities of daily living scale (IADL; Lawton & Brody, 1969). The IADL scale contains instrumental everyday activities, i.e., ability to use telephone, shopping, food preparation, housekeeping, laundry, mode of transportation, responsibility of one' own medications and ability to handle finances (Lawton & Brody, 1969). Measures of IADL are sensitive to stroke-related disability. Performance particularly on finances, shopping, medication management and cooking are shown to be impaired among stroke survivors, and these deficits may be associated with problems on neuropsychological domains like attention, executive functions and memory (Sadek, Sticker, Adair & Haaland, 2011).

Exact clinical determinants of stroke-related functional outcome are not clear yet. However, studies support the significance of neurological status measured with National Institutes of Health Stroke Scale (NIHSS) in the early poststroke phase, and the age of the patients when predicting the ADL outcome beyond 3 months after stroke (A review: Veerbeek, Kwakkel, van Wegen, Ket & Heymans, 2011). Nevertheless, the presence of cognitive impairment after stroke seems to have important functional consequences for stroke patients' independence in physical abilities (Pohjasvaara et al., 1998b; Tatemichi et al., 1994). Even mild cognitive decline has an independent effect on long-term poor functional outcome (Pohjasvaara et al., 2001a). Specifically, impairments on executive functions are associated with both basic activities of daily living and more complex instrumental activities of daily living (Pohjasvaara et al., 2002).

1.1.2 Poststroke cognitive impairment

Poststroke cognitive impairment is a decline in any cognitive domain after stroke. In a Finnish stroke cohort, 62% of stroke patients showed cognitive impairment in at least one cognitive domain three months after stroke (Pohjasvaara et al, 1997). In this cohort 54 % of stroke survivors had deficits in short-term memory, 39 % in constructional and visuospatial abilities, 39 % in executive functions, 25 % in attention, 21 % in abstract thinking, and 17 % in speech, assessed with neuropsychological methods (Pohjasvaara et al., 2001b). Vascular cognitive impairment encompasses all cognitive deficits and changes in behavior associated with all the vascular diseases from mild cognitive impairment to dementia (Gorelick et al., 2011). Thus, poststroke cognitive impairment is regarded as a category of vascular cognitive impairment (O'Brien et al., 2003).

In general, advanced age increases the frequency of cognitive decline among stroke patients (Pohjasvaara, 1997). In addition, lower education, prestroke cognitive decline and functional dependence interact with poststroke cognitive impairment (Leys, Hénon, Mackowiak-Cordoliani & Pasquier, 2005; Mok et al., 2004). Cortical location (Nys et al., 2007) or anterior location (Tay, Ampil, Chen & Auchus, 2006) of stroke might be associated with emergence of cognitive deficits. Nevertheless, there is evidence that patients with subcortical infarcts may develop similar cognitive deficits compared to patients with cortical infarcts (Turunen et al., 2013). Damage of deeper regions such as thalamus, basal ganglia and angular gyrus may likely result in cognitive impairment, but the exact regional factors remain unclear (Gorelick et al., 2011). However, the nature of cognitive impairment depends on the original function of infarcted tissue (Gottesman & Hillis, 2010).

In an epidemiologic study (Kelly-Hayes et al., 2003), 46 % of stroke patients had cognitive deficits six months after stroke. In a recent study, the severity of poststroke cognitive impairment predicted inability to return to work (Kauranen et al., 2013b). In fact, cognitive dysfunction is argued to be a major predictor of functional impairment and higher morbidity resulted from stroke (Oksala et al., 2009; Gottesman & Hillis, 2010).

1.2 Executive functions

The concept of executive functions is applied to describe the processes by which different cognitive functions are combined for goal-directed action. These higher cognitive abilities are responsible for the planning, initiation, sequencing and monitoring of complex target-oriented behavior (Royall et al. 2002). Executive functions reflect the self-regulative controlling the execution of actions related to goal-realization (Eslinger & Chakara, 2004); these functions are responsible for voluntary regulation of perception, memory functions, motor skills and emotional control (Alvarez & Emory, 2006). When executive functions are intact, a person can still be more or less independent despite impairment in a specific cognitive function; whereas with impaired executive functions applying otherwise intact cognitive abilities can remain fragmentary (Jurado & Rosselli, 2007; Lezak, 1982). Thus, impairments in executive functions tend to affect all aspects of behavior. It is reasonable to argue that executive functions are necessary for human adaptive behavior (Jurado & Rosselli, 2007).

There has been debate about the sub-components of executive functions (Diamond, 2013; Jurado & Rosselli, 2007). Historically, propositions of executive functions as controlling “central executive” (Baddeley & Hitch, 1974) to monitoring regulative “supervisory attention system” (Norman & Shallice, 1986) have been presented. Lezak (1982) defines executive functions to contain four components: goal formulation and volition, planning, carrying out goal-directed actions and effective performance. In practice, executive functions or abilities allow us to shift our mindset quickly and adapt to diverse situations, while inhibiting inappropriate behaviors in constantly changing everyday environment (Jurado & Rosselli, 2007). Basic working processes for executive activities include task setting, initiation of the task, detecting errors and behavioral self-regulating functions (Stuss, 2007). The question whether executive functions are controlled by a single ability, or by the components related to each other but still distinct processes, remains unclear (Jurado & Rosselli, 2007; Royall et al., 2002).

1.2.1 Executive functions and brain structures

Early observations of patients with frontal lobe damages were the basis for the research concerning executive functions and their neural correlates (Royall et al., 2002; Samson & Barnes, 2013). Later neuroimaging has supported engagement of the frontal lobes on executive tasks (Royall et al., 2002; Samson & Barnes, 2013; Jurado & Rosselli, 2007), although other brain areas may also participate in similar tasks (A review: Hoffmann, 2013). Prefrontal cortex has several unique qualities, which make it possible to mediate executive control. Prefrontal cortex is connected with more numerous brain regions than any other cortical area: It receives cortical input from other heteromodal association areas and from limbic structures (e.g. Hoffman, 2013; Miller, 2000). In addition, basal ganglia-thalamocortical circuits send major input to prefrontal cortex (Alexander et al., 2012; Royall et al., 2002). Thus, the frontal lobes can integrate and combine motivational, emotional, somatosensory and external sensory information into goal directed, effortful action.

Proposed functionally specialized divisions of executive functions and their anatomical correlates derive from prefrontal structures (Chow & Cummings, 2007). Three frontal-subcortical circuits are particularly relevant for executive functions: dorsolateral prefrontal circuit, lateral orbitofrontal circuit and anterior cingulate circuit (Chow & Cummings, 2007; Royall et al., 2002). These frontal-subcortical circuits are based on subcortical white matter tracks, which connect prefrontal areas to basal ganglia and thalamic structures; connections are reciprocal and have feedback connections back from lower structures to frontal lobes (Figure 1) (e.g. Cummings, 1995). Circuits are located near to each other and have direct activating and indirect inhibitive pathways, which have their effects via thalamus on activity of prefrontal cortex (Chow & Cummings, 2007). Dysfunction in the direct pathway causes abnormal thalamic inhibition, whereas dysfunction in the indirect circuit leads to thalamic overactivity through disinhibition (e.g. Tekin & Cummings, 2002). At cortical level, these executive circuits have reciprocal connections to each other and to association areas in parietal, occipital and temporal lobes, which in turn participate in processing and storing the modal information (Chow & Cummings, 2007). In each hemisphere, each set of circuits is present (e.g. Tekin &

Cummings, 2002). At cortical level, circuits appear to be separated and thus cortical lesions may impair only one circuit and related behaviors; however, subcortical circuits share more proximity, and thus, subcortical pathology is likely to damage several circuits simultaneously leading to mixed syndromes (Royall et al., 2002). Due to this network connectivity, damage to non-frontal brain region may also induce impairments on executive functions (e.g. Stuss, 2007).

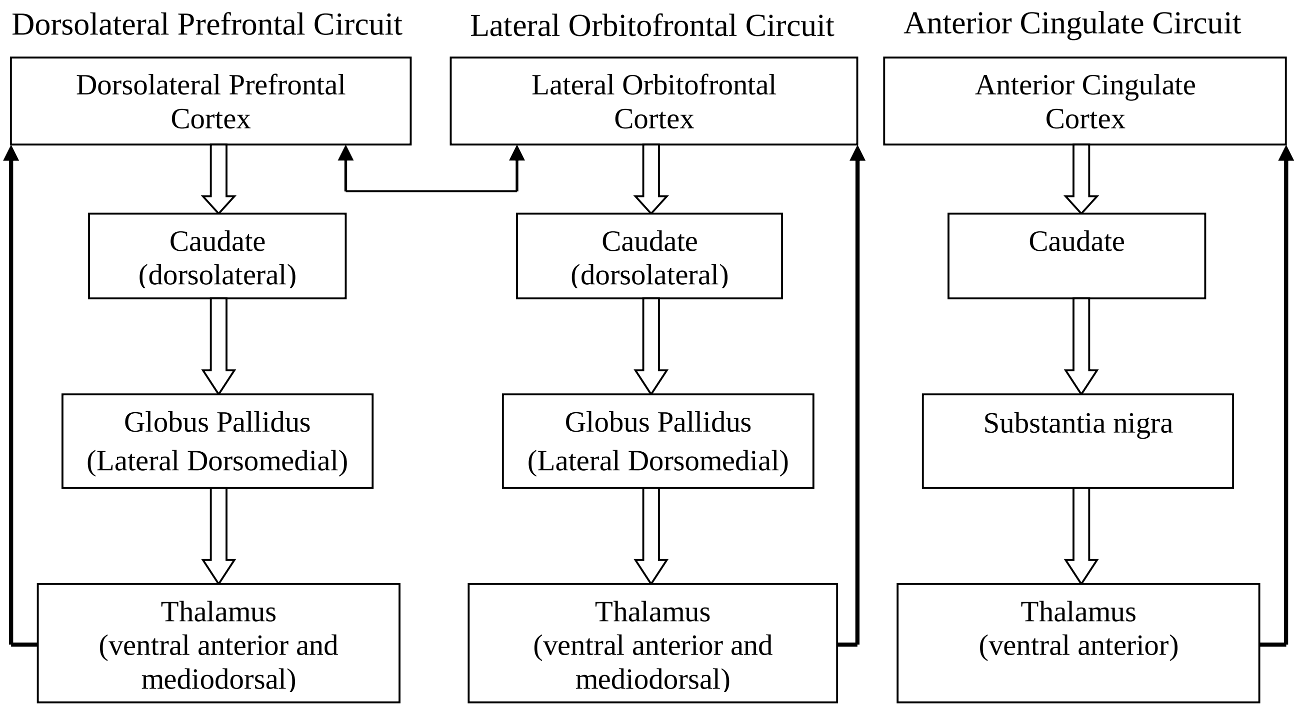

Figure 1. Anatomy of the three frontal-subcortical circuits. Modified after Tekin & Cummings, 2002.

The blood supply of dorsolateral prefrontal circuit comes from middle cerebral artery. Lesion to this circuit is associated with impairment in executive functions such as goal selection, planning and sequencing action, response set formation, set shifting, verbal and spatial working memory, self- monitoring, and self-awareness (Chow & Cummings, 2007; Cummings & Miller, 2007; Jurado & Rosselli, 2007; Royall et al., 2002). The feeding artery of anterior cingulate circuit is anterior cerebral artery. The anterior cingulate is a significant structure for monitoring one’s behavior and for error correction of one’s actions (Chow & Cummings, 2007; Royall, 2002). Lesions of this region may further lead to apathy and amotivational behavior (Chow & Cummings, 2007). Orbitofrontal circuit receives blood supply from two arteries: anterior cerebral artery is the feeding artery for medial part of the circuit, and the middle artery for lateral region of orbitofrontal circuit. In general, orbitofrontal circuit mediates empathic and socially appropriate behavior (Chow & Cummings, 2007). Patient with lesion in this circuit may seem irritable and have poor self-regulation and emotional control due to dysregulation of affective and social behavior. In addition, intact orbitofrontal areas may be necessary for appropriate risk assessment and for inhibition of irrelevant actions (Chow & Cummings, 2007; Royall et al., 2002).

1.2.2 Executive functions and aging

Changes in cognition are a part of normal aging process (Samson & Barnes, 2013; Jurado & Rosselli, 2007; Carey et al., 2008). The elderly differ in their ability to maintain cognitive functions; however, these normal changes are gradual, mild in severity and predictable (Daffner, 2010). There is a decline in the volume of prefrontal cortex due to increasing age, and thus cognitive processes relying on the frontal cortical areas are vulnerable to aging (Samson & Barnes, 2013). Particularly the frontal-subcortical circuits may be susceptible to the effects of aging (Pugh & Lipsitz, 2002), which can predict changes on executive functions; subcortical changes in the white matter are associated with executive functions' deficits in the elderly (Jokinen et al., 2007; Carey et al., 2008).

Decline in working memory (e.g. Alexander et al., 2012), attentional processes (e.g. Hedden et al., 2012) and planning (Andrés & Van der Linden, 2000) are parts of normal aging. In addition, reasoning and problem solving abilities as well as set switching are established to decline in the elderly (Alexander et al., 2012; Darowski, Helder, Zacks, Hasher & Hambrick, 2008; Hedden et al., 2012; Jurado & Rosselli, 2007). Also, the impact of aging on inhibition processes is apparent (Jurado & Rosselli, 2007; Andrés & Van der Linden, 2000). These age-related deficits are likely to show decline in performance on the tests of executive functions (e.g. Samson & Barnes, 2013; Jurado & Rosselli, 2007). The normative cognitive aging is defined as representing a level of neuropsychological functioning that falls within 1.5 or 2 standard deviations of the mean for age (Daffner, 2010). Thus, separating the normal cognitive aging from pathological one can be challenging.

Impairments on executive functions are frequent in elderly stroke patients also without dementia (Ballard et al., 2003; Pohjasvaara et al., 2002). Volume of damaged brain tissue (Vataja et al., 2003) and the number of infarcts and infarct's concentration on left hemisphere (Patel et al., 2002; Vataja et al., 2003) may predict problems particularly on executive functions. However, Zinn and colleagues (2007) did not find association between stroke severity and executive dysfunction. Executive dysfunctioning may further predict poorer functional outcome on complex (Mok et al., 2004; Pohjasvaara et al., 2002) and even basic activities of daily living (Mok et al., 2004). Furthermore, impairments on executive functions may reduce patients' benefits of stroke rehabilitation (Mok et al., 2004; Paolucci et al., 1996). Executive dysfunction may be the primary cognitive feature that differentiates vascular pathology of cognitive decline from Alzheimer disease (Desmond, 2004).

1.2.3 Assessment of executive functions

Correct identification of executive dysfunctioning is crucial in order to understand patients' deficits. Problems at any state of behavioral sequencing may be erroneously interpreted as laziness, lack of motivation or even psychiatric disturbances (Lezak, 1982). However, examining executive functions is difficult. In formal neuropsychological examination the situation and the tests are highly structured, and do not necessary require independent strategy formation through planning and sequencing behavior, i.e., actions that would reveal decreased executive abilities.

Some of the traditional neuropsychological assessment methods of executive functions are Trail Making test, Stroop test, Wisconsin card sorting test (WCST) and Verbal fluency task (Lezak et al., 2012; Royall et al., 2002; Stuss, 2007). These tests examine different aspects or components of executive functions, and are clinically established assessment methods. The Trail Making test (Reitan, 1958) includes two parts, and is used for assessing flexible action shifting and simultaneous processing of two different tasks (Stuss, 2007; Alvarez & Emory, 2006). The Wisconsin card sorting test (Berg, 1948; Grant & Berg, 1948) provides information about set shifting and maintenance, inhibition and rule detection as well as concept formation (Jurado & Rosselli, 2007) and abstraction (Cummings & Miller, 2007). The Stroop test (Stroop, 1935) examines the ability to suppress habitual, automatic responses, i.e., inhibition (Lezak, et al., 2012, p. 365–367; Miller & Cummings, 2007; Jurado & Rosselli, 2007). Performance in the Verbal fluency task is used to assess productivity and initiative as well as volition (Cummings & Miller, 2007).

This task-based approach is useful in identifying impaired capacities, abilities and processes in frontal lobe patients (Jurado & Rosselli, 2007). However, interpretation derived from test results must be done with caution; these tests are multifactorial by nature and individuals can fail for many different reasons (Stuss, 2007). In addition, successful test performance requires several intact cognitive abilities separate from executive functions, e.g. attention, working memory, language skills, or perception. Executive functions tests assess several different executive processes simultaneously. It is rare that a failure in a specific executive functions test would implicate a single, unique executive process (Cummings & Miller, 2007). In other words, each component of executive functions may be impaired independently, but the executive tests may not be specific enough to detect separate failures (Cummings & Miller, 2007; Stuss, 2007).

The Hayling test, Design fluency task and Questioning task are some of the less common executive functions tests in clinical use, and are not widely studied. A few studies with different types of brain damaged patients have used these tests for evaluating executive functions (e.g. Burgess & Shallice, 1996; Jones-Gotman, 1990; Laine & Butters, 1982; Odhuba, Broek & Johns, 2005). However, there are no previous studies considering the feasibility of the Hayling test, Design fluency task and Questioning task in stroke population, even though the poststroke executive dysfunctioning is common. In the following, these three methods are introduced in detail, and the previous findings with different frontal damages are shortly overviewed.

Hayling test

The Hayling sentence completion test was originally developed for studying verbal response suppression and initiation in patients after frontal lobe damage (Burgess & Shallice, 1996). In this test 30 sentences are presented to subjects with the last word omitted. The sentences have been originally chosen so that there is a high probability a particular response to occur (Burgess & Shallice, 1996). In the first condition, subjects' task is to complete 15 sentences with an appropriate word as quickly as possible (e.g. "He sent a letter without…" while appropriate word as an answer would be "a stamp" or "an address"). In the next condition, subjects' task is to complete 15 new sentences again as quickly as possible with a word completely unrelated to the meaning of the sentence, and so the word being inappropriate to context (e.g. "Captain wanted to stay in the sinking…" while inappropriate word would be any word outside the category of vehicles).

The first, automatic condition is thought to reflect automatic response initiation with the appropriate word being context driven (Burgess & Shallice, 1996; Borella, Ludwig, Fagot & De Ribaupierre, 2011) and semantically supported (Belleville, Rouleau & Van der Linden, 2006). In the second part, the context of the sentence could be seen as interference. Thus, the sentence completion with the context-unrelated word requires inhibition of the automatic semantically activated response (Burgess & Shallice, 1996; Borella et al, 2011). Typically, the time difference between response latencies in two conditions is thought to reflect the time needed for the inhibition of the automatic response and for unusual word retrieval (Burgess & Shallice, 1996).

The Hayling test is thought to reflect executive functions, since, it has been shown that patients with frontal lesions have greater difficulties in suppression of habitual response, and thus failing and being slower in the inhibition condition (Burgess & Shallice, 1996). Furthermore, the inhibition condition has shown to be associated with greater activation in the left prefrontal areas (Nathaniel-James, Fletcher & Frith, 1997; Collette et al., 2001). Previous studies have also shown that some specific age related neurodegenerative diseases are associated with poor overall performance on the Hayling test (e.g. Belleville et al., 2006). There is evidence that response latencies between the automatic and inhibition conditions differ significantly more among elderly subjects people compared to younger ones, but the actual inhibition errors are only mildly increased with age (Belleville et al., 2006). In addition, performance on the Hayling test has been associated with traumatic brain injury patients' ratings of their own disability (Odhuba et al., 2005). There are no analogous previous studies done with stroke population.

Design fluency

The Design fluency task was originally developed by Jones-Gotman and Milner (1977) as a nonverbal analog for the Verbal fluency task. The original version of the Design fluency task had two conditions: In the free condition the subject's task is to draw imaginary abstract shapes, that are not nameable or actual objects, and that are not solely abstract scribbles either. In the fixed condition subjects were asked to draw four-line drawings (acceptable lines could be straight or curved). The specific advantages of each condition are not fully understood yet (Kingery et al., 2006). The fixed condition might be more sensitive to right hemisphere dysfunction (Ruff et al., 1994) or frontal lobe function as a whole (Baldo, Shimamura, Delis, Kramer & Kaplan, 2001; Jones-Gotman & Milner, 1977). It has been shown that performance on these two conditions of the task is correlated in healthy subjects (Demakis and Harrison, 1997). The Design fluency task has not become a common neuropsychological assessment method in clinical use, though it's scoring and rater-reliability has been proved to be at least good in the fixed condition (Kingery et al., 2006).

The Design fluency task has been used in several studies to examine effects of aging on productivity and perseveration tendency, thus on executive functioning. Daigneault and Braun (1993) reported the tendency for perseverative responses to increase with age. Also contrary evidence has been reported (Daigneault, Braun & Whitaker, 1992). It has also been shown that productivity in the Design fluency task significantly diminishes with age (Mittenberg, Seidenberg, O'Leary & DiGiulio, 1989). However, these results come from using the free condition. Thus, the normal aging effects on fixed condition remain unclear. There is evidence that patients with mixed frontal lesions produce more perseverative responses (Jones-Gotman, 1990; Levin, Goldstein, Williams & Eisenberg, 1991) and lack productivity (Levin et al., 1991) in the fixed condition. In a recent Korean longitudinal study examiners found inferior performance on the fixed condition of the design fluency task in a cognitively impaired aging group compared to cognitively normal group of the same age (Chi et al, 2012). However, studies of stroke survivors' performance on the Design fluency task are lacking.

Questioning task

The Questioning task, also referred as Identification of common objects (Laine & Butters, 1982), Object identification task (Heindel, Salmon & Butters, 1991) or 20 Questions game (Lezak et al., 2012, p. 578), was originally introduced by Laine and Butters (1982). In the Questioning task, the participant is shown drawings of common objects representing categories such as toys, animals, clothing, manufactured objects etc. The examiner is thinking one of the objects and subject's task is to find it out by asking as few questions as possible (Laine & Butters, 1982). Questions have to be of the type that the examiner can answer only "yes" or "no. The subject is advised to consider what type of questions would lead to the target with as few questions as possible (Laine & Butters, 1982).

It has been shown that patients with frontal lobe damage caused by alcohol (Laine & Butters, 1982; Heindel, Salmon & Butters, 1991) and patients with frontal dysfunction due epilepsy (Upton & Thompson, 1999) use inefficient strategies and make more errors (Upton & Thompson, 1999) on the Questioning task compared to healthy subjects or patients with lesions elsewhere in the brain. Amount of controlled studies using this method is, however, limited; the strategy formation in the Questioning task of stroke patients has not been previously studied.

1.2.4 Executive functions and functional abilities

Executive dysfunction has been found to predict poor poststroke overall survival (Melkas et al., 2010). Complex by their nature, intact executive functions are critical for functional independence in everyday activities. In particular, executive functions are related to self-reported and observed functional abilities in the elderly (Grigsby et al., 1998). In a stroke cohort study, Pohjasvaara and colleagues (2002) found a clear correlation between executive dysfunction and both basic functional abilities (ADL) and more complex functional abilities (IADL). The same results can be derived from the study of patients with traumatic brain injury. Independence on IADL functions was correlated with executive functioning (Bottari, Dassa, Rainville & Dutil, 2009). However, the predictive value of separate executive functions assessment methods on functional abilities in stroke population has not been previously documented.

1.3 The aims of the study

Cognitive impairment is a common poststroke cause of disability. Particularly executive functions have been previously found to be critical in functional abilities of stroke survivors. Increasing age itself effects executive functions, and differentiating the pathological changes from normal aging is important. However, there is no golden standard for measuring executive functions: Sensitivity and specificity of the traditional assessment methods are still insufficient. Non-conventional tests of executive functions, i.e. the Hayling test, Design fluency task, and Questioning task, have not been previously studied in elderly stroke population. The aim of this study is to examine which of the traditional and less common executive functions tests are the most sensitive in clinical assessment of executive functions: Do these non-conventional tests offer an added value on evaluating executive functions, and how the performances on these tests predict the functional abilities in a clinical stroke population.

Research questions:

1) Which of the three non-conventional (i.e., the Hayling test, Design fluency task and Questioning task), and established (i.e. the Trail Making test, Stroop test, Wisconsin card sorting test, Verbal fluency task) tests of executive functions most clearly differentiate elderly ischemic stroke patients from healthy elderly control subjects?
2) How do the less common tests correlate with the established tests of executive functions in the sample of elderly ischemic stroke patients?
3) What is the predictive value of the different executive functions tests on basic and more complex functional abilities three months after stroke and at 15 months follow-up?

2 METHODS

2.1 Subjects and study protocol

The original Helsinki Stroke Aging Memory Study (SAM) included 486 ischemic stroke patients, aged 55–85 (Pohjasvaara et al., 1997). The patients were admitted consecutively to the emergency unit of Helsinki University Central Hospital. Three months after the index stroke, 451 patients went through clinical neurological and mental status examinations. The exclusion criteria for these mentioned examinations were refusal (n = 1), reduced level of consciousness (n = 1), hearing impairment (n = 1) and obvious problems in understanding or producing speech (n = 32). Of these 451 patients, a detailed neuropsychological examination was completed on 409 patients. The exclusion criteria for the neuropsychological examination were refusal, severe disorientation or delirium, poor knowledge of Finnish language, severe sight impairment, aphasia, and lack of co-operation.

For an additional examination focusing on executive functions, a total of 107 subjects were taken consecutively from the original sample that participated in the initial comprehensive neuropsychological examination. The exclusion criteria were not completing the initial neuropsychological examination (n = 13), refusal (n = 13), lack of co-operation (n = 2) and other reasons (n = 17). Thus, for the present study, 62 ischemic stroke patients underwent the neuropsychological examination focusing on executive functions. The initial comprehensive neuropsychological assessment was conducted approximately three months after stroke (mean = 103 days, SD = 12.7). Subjects underwent the additional examination in a few weeks after participating in the initial assessment.

The same neuropsychological examinations were also carried out for 39 neurologically healthy control subjects. These control subjects were derived from an earlier population based study (Helsinki-Vantaa aging study; Ylikoski et al., 1993).

2.2 Neuropsychological assessments

The initial comprehensive neuropsychological examination covered several cognitive domains including orientation, attention, abstract thinking, reasoning, problem solving, executive functions, the speed of mental processing, motor functions, speech functions, visuoperceptual functions, counting, reading and writing. The present study focuses on executive functions. Executive functions were initially examined with the Trail Making test, Stroop test, Wisconsin card sorting test and Verbal fluency task. The methods used were clinically established neuropsychological tests (Lezak et al., 2012), and had been used in previous studies of the SAM cohort (e.g. Jokinen et al., 2006; Leskelä et al., 1999). The tests were administered by following the standard instructions and scorings. In addition, the global cognitive status was examined with Mini Mental State Examination (MMSE).

The purpose of the present study was to examine non-conventional executive functions tests with stroke patients. Therefore a subsample went through further neuropsychological examination at a second visit approximately three months poststroke. The Hayling test, Design fluency task and Questioning task were completed by 62 stroke patients and 39 control subjects. Scoring the tests was conducted by two independent assessors, and the inter-rater correlations for each of these tests were calculated.

Hayling test

A Finnish translation of the original Hayling test was used according to original instructions (Burgess & Shallice, 1996). The participants were asked to listen to the sentence read by the examiner and immediate provide the last word. Two practice sentences were presented before the actual test. If the participant gave an erroneous response to the example sentences, the examiner repeated the test instructions, but during the actual test, errors were not corrected. Response latencies were recorded. If the subject had not produced a response within 60 seconds, the trial was terminated and a response latency of 60 seconds was recorded. In the inhibition condition error scores were scored according to the criteria proposed by Burgess and Shallice (1996): Participants received zero points when an unrelated word was provided, one point when subject provided a response semantically related to the sentence, and a three point error score was obtained when the sentence was completed with an appropriate, context fitting word. For the automatic condition, the analogous scoring system using reversed criteria was developed: three points were given when subject completed the sentence with an unrelated word, one point when the word was semantically related to the sentence context and zero points when the target word was provided. Thus, a larger score was associated with more severe impairment.

Design fluency

Subjects were asked to draw as many four-line drawings as they can in 60 seconds. Two example figures were shown to subjects, and they were asked to draw one example on their own before the actual test. Straight and curve lines connected or separated to each other were accepted. The number of acceptable drawings, perseverative errors and test rule violations (i.e. drawings with less or more than four-lines) were scored.

Questioning task

A 21 x 30 cm card displaying 42 drawings of common objects such as animals, buildings, plants and tools (Laine & Butters, 1982), was represented to the subjects. Subjects were told that it is a kind of a game in which the examiner is thinking of one of the objects and subject's task is to find the object the examiner was thinking of by asking as few questions as possible. Subjects were also told that the questions can be answered only "yes" or "no". Before the actual test subjects were asked to name the pictures, and if incorrect naming occurred, subjects were corrected. There was no time limit to complete the task but only the first six questions were scored. The number of Constraint seeking questions (e.g. "Is it an animal?"), Pseudo-constraint questions (which refer to a specific object as if it was constraint seeking without reducing alternative objects; e.g. "Does it bark?"), Hypothesis testing questions ("Is it a dog?"), perseverative questions, unnecessary questions (which refer to new question without giving any new information; e.g. before subject has asked "Is it manufactured?" and then asks if "Is it some kind of tool?"), and wrong questions (i.e. rule breaking questions) were scored.

2.2 Functional abilities

Functional abilities in daily living were assessed with modified Rankin Scale (mRS) (Banks & Marotta, 2007; Rankin, 1957) three months poststroke. The scale is ordinal and defines seven levels of disability from 0 "no disability" to 5 "severe disability", the seventh level being "death" (Table 1). The assessments were made as self-ratings or ratings by a family-member. Modified Rankin Scale was used again 15 months after the stroke for assessing the long term, and thus more stable dependency. Assessment at 15 months was performed as phone interviews.

Table 1. Modified Rankin Scale (mRS)

mRS-score	Description
0	No symptoms
1	No significant disability despite symptoms; able to perform all usual duties and activities.
2	Slight disability; unable to perform all previous activities but able to look after own affairs without assistance.
3	Moderate disability; requires some help but able to walk without assistance
4	Moderately severe disability; unable to walk without assistance and unable to attend to own bodily needs without assistance
5	Severe disability; bedridden, incontinent, and requires constant nursing care and attention.
6	Death

More complex activities of daily living were assessed with Lawton's scale for instrumental activities of daily living (IADL) (Lawton & Brody, 1969) three months after the stroke. Lawton's IADL scale consists of eight domains, which each assess one particular complex function, e.g. "Can handle finance issues independently" (Appendix 1). For each question score 1 indicates independent functionality and score 0 dependency on help. Total score ranges from 0 to 8.

The National Institutes of Health's Stroke Scale (NIHSS) was used to assess the severity of neurological symptoms caused by a stroke. NIHSS consists of 11 items, each of which scores a specific ability. Scores vary from 0 to 2, or to 3, or to 4, depending on item (Appendix 2). For each item 0 indicates normal function while a higher score indicates a higher level of impairment. Scores from each item are summed in order to calculate the total NIHSS score. The highest total score in NIHSS is 42.

2.3 Statistical analyses

The statistical analyses were performed with the SPSS 22.0 package for Windows. The number of missing values in neuropsychological tests ranged from 0 % to 15.8 % of the subjects, the largest percentages occurred in the Trail Making test B. The occurrence of missing values was associated with clinical severity of stroke as rated with NIHSS, and was most often caused by patient's inability to complete the entire test battery. Missing values were not replaced.

Error scores and times spent in each test were included in analyses. However with the Trail Making test the number of correct answers were divided with the time spent (score/time) in both parts of the test separately to avoid the effects of different tactics (slow with correct answers or fast with many errors) on outcome (e.g. Vataja et al., 2003). Time differences between the Trail Making test A and B, Stroop test part A (i.e. colour naming condition) and B (i.e. colour interference condition), and Hayling test part A and B were calculated.

The group differences in demographic variables were analyzed with independent samples t-test and with non-parametric Chi-square test where appropriate. Neuropsychological test performance between groups was compared with independent samples t-test and non-parametric Mann-Whitney U-test. To consider multiple comparisons from co-dependent data, more conservative p-value, i.e. 0.01, was used to test statistical significance. Correlations between neuropsychological tests were calculated with Pearson's r for continuous variables, and Spearman's ordinal r was used as a non-parametric equivalent.

MRS and IADL scale scores were recoded. MRS scores from 0 to 2 were coded as "independent" and functional dependence was defined as mRS = 3–5 indicating moderate to severe disability and need for assistance in daily activities (Table 1) (Jokinen et al., in press). IADL scores 7-8 were coded as "independent" and 0-6 as "dependent" similar to mRS variable recoding. The link between executive functions test performance and functional abilities was analyzed by forming separate independent logistic regression models. In these models, functional abilities and instrumental activities of daily living in the stroke group were predicted by one test variable at a time. At block 1 demographic variables (age, sex and education) were controlled, at block 2 further NIHSS scores were added into the models.

3 RESULTS

3.1 Demographic variables and inter-rater correlations

There were 32 males and 30 females in the stroke group, and 18 males and 21 females in the control group. Comparison of demographic variables (i.e. sex, age and education) and MMSE between groups is presented in Table 2. There were no significant differences between the stroke and the control group in demographic variables. The control group received higher scores on MMSE compared to the stroke group ($p < .001$), the difference between groups being 1.84 points. In the stroke group, clinical stroke severity was 1.94 on average (SD = 3.10) ranging from 0 to 17 (Tables 2 and 3). The inter-rater correlations for the scores of the Hayling test, Design fluency and Questioning task varied from 0.93 to 0.99 indicating excellent inter-rater agreement.

Table 2. Demographic variables between groups

	Stroke				Control				p
	Mean	SD	Min	Max	Mean	SD	Min	Max	
Age	68.44	7.33	55	85	67.45	5.32	61	76	.49
Education[1]	7.84	4.73	0	28	9.41	3.54	5	20	.08
MMSE	26.34	2.92	20	30	28.16	2.06	22	30	<.001
NIHSS	1.94	3.10	0	17					

[1]Total education in years; includes comprehensive school and occupational studies.
MMSE = Mini Mental State Examination; NIHSS = National Institute of Health Stroke Scale.

Table 3. National Institutes of Health's Stroke Scale (NIHSS) scores

NIHSS	n (%)
0	27 (43.5)
1–4	26 (41.9)
5–15	8 (12.9)
16–20	1 (1.6)
21–42	0

3.2 Group differences on executive functions test performance

Comparison between groups on executive functions tests are presented in Table 4. Seven test variables met the conservative criteria for significance value: Performance on Hayling B, Trail Making B, Stroop test, WCST, Verbal fluency for category and for letter, and the number of Constraint seeking questions in Questioning task differed between stroke and control group ($p \leq .01$). The groups did not differ on the time variables of the Hayling test and the Stroop test, or on the performance in the Trail Making A, or Design fluency task. In the Questioning task control subjects asked more Pseudo-constraint questions compared to stroke group (1.21 versus 0.67, p = .026) and stroke group asked more Hypothesis testing questions (2.05 versus 1.18, p = .041) but these differences were considered as non-significant. In addition, the stroke patients made significantly more perseverative errors in tests of executive functions in total compared to control group (10.24 versus 5.34 respectively; p < .001).

Table 4. Performance on the tests of executive functions in stroke patients and control subjects

Test variable	Stroke (mean ± sd)	Control (mean ± sd)	t	p
Hayling A, time	49.84 ± 33.28	39.46 ± 26.45	1.65	.103
Hayling, time difference	65.59 ± 68.10	38.49 ± 47.48	2.17	.032
Hayling B, error score	10.82 ± 9.27	3.49 ± 3.32	549.00[1]	<.001
Trail Making A (score/time)	0.36 ± 0.18	0.45 ± 0.17	-2.44	.017
Trail Making B (score/time)	0.11 ± 0.08	0.16 ± 0.10	-2.73	.008
Stroop A, time	22.03 ± 11.97	18.42 ± 4.91	1.77	.038
Stroop, time difference	25.57 ± 15.02	19.03 ± 14.69	2.11	.038
Stroop B, number of errors	3.07 ± 5.61	0.16 ± 0.44	713.00[1]	<.001
WCST, correct	20.11 ± 11.15	27.79 ± 10.72	651.00[1]	.001
Verbal fluency, category	17.24 ± 6.69	20.58 ± 4.62	-2.95	.004
Verbal fluency, letter	11.13 ± 5.76	14.92 ± 4.35	-3.47	.001
Design fluency, correct	4.51 ± 2.17	5.37 ± 2.83	915.00[1]	.065
Questioning task, CS	2.35 ± 2.34	3.42 ± 2.23	836.00[1]	.010
Questioning task, PC	0.67 ± 1.25	1.21 ± 1.66	918.00[1]	.026
Questioning task, HT	2.05 ± 2.45	1.18 ± 1.98	921.00[1]	.041
Total perseverative errors	10.24 ± 6.80	5.34 ± 5.84	554.00[1]	<.001

[1]Mann-Whitney U-test. CS = Constraint seeking questions; PC = Pseudo-constraint questions; HT = Hypothesis testing questions; WCST = Wisconsin card sorting test.

3.3 Correlations between tests of executive functions

Spearman’s correlation coefficients between test score variables and Pearson’s correlation coefficients between test time variables are presented in Tables 5 and 6. The Hayling test error score correlated moderately and positively with number of errors in the Stroop test (Table 5). The time spent in these two test’s part A’s shared also moderate correlation (Table 6). Correlation between time differences in the Hayling and the Stroop test was close to zero. Design fluency task shared a strong correlation with Verbal fluency for category and for letter (Table 5), and also a strong correlation with Wisconsin card sorting test.

In Questioning task there was a strong negative internal correlation between the use of Constraint seeking questions and Hypothesis testing questions and between the use of Hypothesis testing and Pseudo-constraint questions (Table 5). Constraint seeking questions correlated negatively with the Hayling test's error score but positively and at least moderately with Wisconsin card sorting test. Hypothesis testing questions shared moderate negative correlation with Wisconsin card sorting test and with Verbal fluency for letter. Pseudo-constraint questions did not share correlation with any other test variable. Total number of perseverative errors shared moderate to strong correlation with every other test variable except Pseudo-constraint questions in the Questioning task (Table 5). Wisconsin card sorting test correlated significantly with every other executive test variables but the Hayling test.

Table 5. Spearman's correlation coefficients between executive functions tests in stroke patients

	Hayling error score	Questioning task, CS	Questioning task, HT	Questioning task, PC	Verbal fluency, category	Verbal fluency, letter	Stroop, number of errors	WCST, correct	Design fluency, correct
Questioning task, CS	-.39**								
Questioning task, HT	.27*	-.73***							
Questioning task, PC	-.09	.25	-.50**						
Verbal fluency, category	-.38**	.38**	-.28*	.18					
Verbal fluency, letter	-.23	.36**	-.34**	.11	.60***				
Stroop, number of errors	.33**	-.31*	.23	-.18	-.38**	-.15			
WCST, correct	-.26	.48***	-.37**	.24	.58***	.29*	-.50***		
Design fluency, correct	-.31*	.37**	-.28*	.24	.58***	.42***	-.27*	.49***	
Total perseverative errors	.30	-.45***	.31*	.10	-.40**	-.30*	-.41**	-.62***	-.30*

*p ≤ .05; **p ≤ .01; ***p ≤ .001.
CS = Constraint seeking questions; HT = Hypothesis testing questions; PC = Pseudo-constraint questions; WCST = Wisconsin card sorting test.

Table 6. Pearson's correlation coefficients between executive functions tests in stroke patients

	Hayling A, time	Hayling, time difference	Stroop A, time	Stroop, time difference	Trail Making A (score/time)
Hayling time difference	-.43				
Stroop A, time	.43***	.16			
Stroop, time difference	-.19	.04	-.09		
Trail Making A (score/time)	-.28*	-.15	-.56***	-.08	
Trail Making B (score/time)	-.40**	-.28*	-.45***	-.18	.63***

*$p \leq .05$; **$p \leq .01$; ***$p \leq .001$.

3.4 Predicting the functional dependence three months poststroke and at 15 months follow-up

Separate logistic regression models for mRS and IADL at three months poststroke are presented in Tables 7 and 8, respectively. In block 1, demographic variables were controlled, and in block 2, NIHSS score was added to models.

Error score in the Hayling test part B, time spent on Hayling test part B, Verbal fluency for category, Design fluency task, Trail Making test and error score in Stoop test part B were significant predictors of the mRS at three months when age, sex and education were adjusted (Table 7). In addition, total perseverative errors predicted on mRS scores three months after stroke. The error score in Hayling test, Verbal fluency for category, Trail Making test A, Stroop test error score, WCST score and total perseverative errors remained significant predictors when NIHSS was additionally adjusted.

The Hayling error score, Verbal fluency for category, Design fluency task and error score in the Stroop test part B predicted IADL at three months when demographic variables were controlled (Table 8). Errors in Stroop test part B and Trail Making A remained significant predictors when NIHSS was added to models.

Executive test performance was further used to predict functional ability on MRS scale at 15 months follow-up after stroke. Results for separate logistic regression models are presented in Table 9. At 15 months poststroke time spent on Hayling test part B had predictive value on functional ability at 15 months in block 1 but the effect disappeared when clinical stroke severity was adjusted to the model. Time-difference between Hayling test part A and B was a significant predictor for mRS scores when demographic variables were controlled and further remained significant when clinical severity of stroke (NIHSS) was controlled.

Table 7. Test performance as predictor of functional dependence 3 months poststroke

		Block 1:Demographic variables included				Block 2:NIHSS additionally included			
				95 % CI for OR				95 % CI for OR	
Test variable	n	B	OR	Lower	Upper	B	OR	Lower	Upper
Hayling A, time	61	.02	1.02	1.00	1.04	0.14	1.01	0.99	1.04
Hayling B, time	61	0.01*	1.01	1.00	1.02	0.01	1.01	1.00	1.02
Hayling, time difference	61	0.01	1.01	1.00	1.02	0.01	1.01	1.00	1.02
Hayling B, error score	61	0.17**	1.18	1.06	1.32	0.23*	1.26	1.04	1.51
Questioning task, CS	61	-0.47*	0.62	0.39	0.99	-0.39	0.68	0.41	1.10
Questioning task, HT	61	0.12	1.13	0.86	1.48	0.10	1.11	0.79	1.55
Questioning task, PC	61	-0.16	0.85	0.44	1.67	0.62	1.86	0.75	4.60
Verbal fluency, category	62	-0.25**	0.78	0.66	0.92	-0.27*	0.77	0.61	0.96
Verbal fluency, letter	60	-0.06	0.95	0.83	1.08	-0.10	0.91	0.77	1.06
Trail Making A (score/time)	60	-20.78**	0.00	0.00	0.00	-24.10*	0.00	0.00	0.02
Trail Making B (score/time)	52	-45.86**	0.00	0.00	0.00	-38.30	0.00	0.00	109.29
Stroop A, time	61	0.27**	1.31	1.11	1.54	0.60*	1.82	1.10	3.01
Stroop B, time	61	0.03	1.03	0.99	1.06	0.02	1.02	0.98	1.07
Stroop, time difference	61	-0.02	0.98	0.93	1.03	-0.02	0.98	0.92	1.04
Stroop B, number of errors	61	0.22**	1.25	1.08	1.44	0.23*	1.26	1.05	1.52
WCST, correct	56	-0.11	0.89	0.81	0.99	-0.13*	0.88	0.78	1.00
Design fluency, correct	60	-0.71**	0.49	0.30	0.80	-0.54	0.58	0.33	1.04
Total perseverative errors	56	0.12*	1.13	1.00	1.27	0.18*	1.19	1.02	1.40

*p ≤ .05; ** p ≤ .01.

CS = Constraint seeking questions; HT = Hypothesis testing questions; PC = Pseudo-constraint questions; WCST = Wisconsin card sorting test.

Table 8. Test performance as predictor of impairment in Instrumental activities of daily living (IADL) 3 months poststroke

		Block 1:Demographic variables included				Block 2:NIHSS additionally included			
				95 % CI for OR				95 % CI for OR	
Test variable	n	B	OR	Lower	Upper	B	OR	Lower	Upper
Hayling A, time	58	0.01	1.01	0.93	1.21	-0.00	1.00	0.97	1.03
Hayling B, time	58	0.01	1.01	1.00	1.02	0.00	1.00	0.99	1.02
Hayling, time difference	58	0.01	1.01	1.00	1.02	0.00	1.00	0.99	1.01
Hayling B, error score	58	0.11**	1.12	1.67	55.26	0.91	1.10	0.99	1.21
Questioning task, CS	58	-0.12	0.88	0.66	1.18	-0.02	0.98	0.68	1.40
Questioning task, HT	58	0.06	1.06	0.83	1.36	0.05	1.05	0.77	1.42
Questioning task, PC	58	-0.29	0.75	0.41	1.36	-0.04	0.96	0.49	1.92
Verbal fluency, category	59	-0.10*	0.90	0.81	1.00	-0.06	0.94	0.83	1.07
Verbal fluency, letter	57	-0.01	0.99	0.89	1.11	-0.05	0.96	0.82	1.11
Trail Making A (score/time)	57	-7.99	0.00	0.00	0.15	-7.43*	0.00	0.00	0.81
Trail Making B (score/time)	50	-6.75	0.01	0.00	30.71	-3.64	0.03	0.00	1010.84
Stroop A, time	58	0.13*	1.13	1.02	1.25	0.61*	1.84	1.11	3.05
Stroop B, time	58	0.03	1.03	0.99	1.07	0.02	1.03	0.98	1.07
Stroop, time difference	58	0.00	1.00	0.96	1.05	0.01	1.02	0.97	1.07
Stroop B, number of errors	58	0.36*	1.43	1.06	1.94	0.50*	1.64	1.03	2.61
WCST, correct	54	-0.03	0.97	0.92	1.03	-0.02	0.98	0.91	1.06
Design fluency, correct	57	-0.44*	0.65	0.45	0.93	-0.26	0.77	0.50	1.18
Total perseverative errors	54	0.09	1.09	0.98	1.21	0.11	1.12	0.98	1.27

*p ≤ .05; ** p ≤ .01.

CS = Constraint seeking questions; HT = Hypothesis testing questions; PC = Pseudo-constraint questions; WCST = Wisconsin card sorting test.

Table 9. Test performance as predictor of functional dependence at 15 months follow-up

		Block 1:Demographic variables included				Block 2:NIHSS additionally included			
				95 % CI for OR				95 % CI for OR	
Test variable	n	B	OR	Lower	Upper	B	OR	Lower	Upper
Hayling A, time	57	0.01	1.01	0.99	1.03	0.00	1.00	0.98	1.02
Hayling B, time	57	0.01*	1.01	1.00	1.02	0.01	1.01	1.00	1.03
Hayling, time difference	57	0.01*	1.01	1.00	1.02	0.01*	1.01	1.00	1.02
Hayling B, error score	57	0.05	1.05	0.98	1.12	0.02	1.02	0.95	1.10
Questioning task, CS	56	-0.07	0.93	0.69	1.25	-0.00	1.00	0.73	1.37
Questioning task, HT	56	0.11	1.12	0.87	1.45	0.08	1.08	0.82	1.42
Questioning task, PC	56	0.04	1.04	0.59	1.83	0.32	1.38	0.73	2.59
Verbal fluency, category	57	-0.03	0.97	0.88	1.07	0.03	1.03	0.93	1.14
Verbal fluency, letter	55	0.01	1.01	0.89	1.14	0.03	1.03	0.90	1.17
Trail Making A (score/time)	55	-5.32	0.01	0.00	1.25	-3.69	0.03	0.00	9.94
Trail Making B (score/time)	48	-6.30	0.00	0.00	180.67	-4.82	0.01	0.00	2001.38
Stroop A, time	56	0.04	1.04	0.98	1.09	0.01	1.01	0.95	1.07
Stroop B, time	56	0.00	1.00	0.97	1.04	-0.00	1.00	0.96	1.04
Stroop, time difference	56	-0.01	0.99	0.95	1.04	-0.00	1.00	0.95	1.04
Stroop B, number of errors	56	0.06	1.06	0.96	1.16	0.02	1.02	0.91	1.14
WCST, correct	51	-0.01	0.99	0.93	1.06	0.01	1.01	0.94	1.08
Design fluency, correct	55	-0.24	0.79	0.56	1.12	-0.05	0.95	0.64	1.43
Total perseverative errors	51	0.07	1.08	0.97	1.19	0.07	1.28	0.93	1.76

*p ≤ .05.
CS = Constraint seeking questions; HT = Hypothesis testing questions; PC = Pseudo-constraint questions; WCST = Wisconsin card sorting test.

4 DISCUSSION

In the present study, the aim was to examine which of the three less common (i.e. the Hayling test, Design fluency task and Questioning task) and established (the Trail Making test, Stroop test, Wisconsin card sorting test, Verbal Fluency task) tests of executive functions most clearly differentiate elderly ischemic stroke patients from healthy elderly control subjects, and how do the less common tests correlate with the established tests of executive functions. In addition, the predictive value of the different executive functions tests on basic and more complex functional abilities three months after stroke and at 15 months follow-up was studied.

It was found, that the stroke patients performed less well compared to control subjects in all of the established tests and most non-conventional tests of executive functions. The Design fluency task was the only test that did not significantly differentiate stroke patients from healthy controls. With all the other used methods, at least one variable of each test differed between stroke patients and control subjects, even when the conservative p-value (i.e. $p \leq .01$) was used. Hence, the used assessment methods clearly differentiated stroke patients from healthy controls. This result is converging with previous results, that executive functions are vulnerable for stroke related impairments (e.g. Patel et al., 2002; Pohjasvaara, 2002; Pohjasvaara, 2001b). Behind this vulnerability of executive functions due to stroke may be their complex neural basis in frontal-subcortical circuits (Gottesman & Hillis, 2010; Zinn, 2007; Chow & Cummings, 2007). The frequency of poststroke cognitive deficits increases with age (Pohjasvaara, 1997). However, subtle changes in cognition and in executive functions are also apparent as a part of normal aging (Samson & Barnes, 2013; Jurado & Rosselli, 2007). Thus, when assessing elderly stroke survivors, the distinction between normal age-related changes and pathological changes, potentially leading to functional disability, is important. In the present study, the results indicate that impairments in executive functions after stroke are detectable with neuropsychological tests even in elderly, although increasing age itself normally causes impairments on executive functions (Samson & Barnes, 2013; Jurado & Rosselli, 2007).

Interestingly, besides the established tests of executive functions, the Hayling test and the Questioning task differentiated stroke patients from healthy controls. This result is novel since these tests have not been previously studied in stroke population. According to the previous findings with different patient populations, patients with frontal lobe damage and possibly with executive dysfunction make more errors in the Hayling test (Burgess & Shallice, 1996) and use inefficient strategy in the Questioning task (Laine & Butters, 1982; Heindel, Salmon Butters, 1991). Although the stroke patients in the present study may not have had damage particularly in frontal parts of the brain, it is reasonable to argue that they performed less well due to impairments in executive functions based on their poor performance on the established tests of executive functions as well. It was also found, that performances on the Hayling and Stroop tests shared at least moderate correlation. The Stroop test has traditionally been considered as reflecting the inhibition and self-controlling aspects of executive functions (Stroop, 1935; Jurado & Rosselli, 2007, Lezak et al., 2012, p. 365–377). Previous studies have proposed the Hayling test to have similar features (Burgess & Shallice, 1996; Nathaniel-James et al., 1997). In the present study, there was a moderate correlation between inhibition errors in the Hayling test and perseveration tendency as well. Perseveration tendency reflects inability to switch strategy and difficulties in efficient strategy formation. Wisconsin card sorting test – assessing particularly switching and strategy formation (e.g. Jurado & Rosselli, 2007) – also correlated negatively with inhibition errors in the Hayling test. This converging evidence proposes the potential of the Hayling test as an assessment method of the self-control and inhibition. In the present data, the Questioning task's Constraint seeking and Hypothesis testing questions correlated with virtually every other executive test. However, Pseudo-constraint questions of the Questioning task did not have common variance with other tests. Surprisingly, healthy control subjects asked more Pseudo-constraint questions compared to the stroke patients, although this difference was not statistically significant. In previous studies, the Pseudo-constraint questions have been associated with poor frontal lobe functioning and inefficient strategy use (Laine & Butters, 1982; Upton & Thompson, 1999). Considering the lack of shared variance with other tests in addition to the surprising result, that control subjects asked more Pseudo-constraint questions compared to stroke patients in this data, Pseudo-constraint questions may not be a reliable correlate of executive functions on its own in elderly stroke patients. Nevertheless as a whole, our results indicate that the Hayling test and the Questioning task are feasible methods for assessing executive functions in stroke population.

As was mentioned above, the Design fluency task was the only test that did not significantly differentiate stroke patients from healthy controls. The Design fluency task may require other cognitive domains besides executive functions. For example, the motor planning, ability to generate novel motor actions and the speed of drawing have been found to contribute to the performance in the Design fluency task (Suchy, Kraybill & Gidley Larson, 2011). Motor actions are known to become slower with increasing age. Thus, the Design fluency may not be sensitive enough to detect differences in executive functions among the elderly over these decreased motor abilities. In addition, the performance in the Design fluency task has been found to recruit both hemispheres in healthy subjects (Elfgren & Risberg, 1998). Hence, the stroke patients with unilateral lesions may compensate the activation loss with the intact hemisphere, and the test performance remains unaffected. In the present data, however, stroke patients' performance on the Design fluency task correlated significantly with Verbal fluency task, as could be expected. The Verbal fluency task has previously been associated with productivity, initiation and strategy formation (e.g. Cummings & Miller, 2007). Productivity in the Design fluency task has previously been found to be diminished with age (Mittenberg et al., 1989), and among the frontal lobe patients (Levin et al., 1991) indicating the possible influence of executive dysfunction. Thus, the same particular sub-components of executive functions could be behind the performances in these tests, even though each of these tests requires also other cognitive abilities (i.e. language skills, motor functions) in addition to executive functions (e.g. Suchy et al., 2011; Baldo et al., 2001). In the present data, the mean number of abstract shapes drawn in the Design fluency task was rather small among the stroke patients but also among the healthy control subjects. This could indicate, that the Design fluency task may have been too challenging for both of the studied groups, and in the present data, it could not reliably specify the different performances among the subjects (i.e. the floor effect).

In addition to the performance on the different executive functions tests, the over-all perseveration tendency – measured with total amount of perseverative errors in the neuropsychological assessment – differentiated stroke patients from healthy control subjects. Perseverative errors on tests of executive functions have previously been linked to age-related changes in cognition (Daigneault & Braun, 1991) but also frontal lobe dysfunction (Jones-Gotman, 1990). Thus, according to the present study, tendency for perseverations may be a sign of vascular-based executive dysfunction even in the elderly, and distinguishable from general age-related changes.

Functional independence is an important outcome of stroke (e.g. Pohjasvaara et al., 1998b). According to previous results, poststroke cognitive deficits are related to functional disability (Pohjasvaara et al., 2001a) and even long-term overall stroke survival (Oksala et al., 2009). In previous studies, especially executive functions are strongly related to basic functional abilities (ADL) and more complex functional abilities (IADL) in the elderly (Pohjasvaara et al., 2002; Grigsby et al, 1998). In the present study, the executive functions were associated with functional dependence (mRS ≤ 2) three months after the index stroke. Interestingly, the Hayling test, Design fluency task and Questioning task were significant predictors of the dependence at three months poststroke. These results are particularly fascinating, since there are no previous studies concerning the relation of these methods with functional abilities. Furthermore, the predictive value of the Hayling test, Verbal fluency task, Trail Making test, Stroop test, Wisconsin card sorting test and tendency for perseverations remained even when the neurologically assessed stroke severity (NIHSS) was controlled. This finding is in line with the previous results that neurologically assessed good clinical recovery does not ensure intact cognition (Kauranen et al., 2013a).

Furthermore, in the present study, the executive functions were associated with dependence in more complex instrumental activities of daily living (IADL $\geq$ 7) assessed three months after the index stroke. This result is converging with previous studies, as mentioned above. More considerably, the non-conventional tests, i.e. the Hayling test and Design fluency task, proved to be significant predictors of these more complex functional abilities. After adjusting for neurologically assessed severity of stroke in the analysis, the Trail Making test and the Stroop test maintained their predictive value on instrumental activities of daily living.

Cognitive deficits are often prolonged among stroke survivors (Kelley-Hayes et al., 2003; Oksala, 2009). In the present study, even at 15 months follow-up, executive functions further predicted the functional dependence. Interestingly, the Hayling test was the only test of executive functions that retained its predictive value in the long-term. Furthermore, the Hayling test remained as a significant predictor of functional dependence even when the stroke severity was controlled. Although the executive functions had predictive value on functional abilities at 15 months follow-up, also the other factors in addition to impaired executive functions may have been important for functional outcome in the long-term. In addition, those who completed the ADL scale 15 months after the index stroke may have recovered better compared to those who did not participate in the follow-up. Thus, differences among this successful-recovery group can be more difficult to find. As a whole, however, results from the present study are converging with previous findings of the predictive value of executive functions on the poststroke basic functional and more complex functional abilities. Furthermore, the less common tests of executive functions had predictive value on the functional dependence. Particularly, the Hayling test proved to most constantly predict the functional dependence, even in the long-term.

The present study has a few limitations. The sample used in this sub-study was relatively small, even though the original SAM cohort was large and well documented. Sample size of the present study restricted the batch of possible statistical methods, and therefore for instance factor analysis could not be used. In addition, due to the nature of executive functions tests, subjects who completed the two neuropsychological assessments may have had better global cognitive functioning compared to those who were excluded. Thus, the differences between studied groups might underestimate the differences at population level. In some neuropsychological tests, data was reduced by missing values (e.g. in Trail Making B 15.8 %), and distributions of different variables could be affected. In the present data, occurrence of missing values was associated with stroke severity (NIHSS). Thus, the most severely impaired patients did not complete the comprehensive assessment of executive functions. As a consequence, effects and predictive value of executive functions on, for example, long-term functional abilities and dependence may be greater in population level compared to the present results. On the other hand, however, besides the small sample size and thus the relatively small statistical power, in the present study the performance on the tests of executive functions was associated with functional abilities and predicted functional dependence in the long-term. This emphasizes the value of executive functions in functional outcome after stroke.

An advantage of this study was the extensive battery of executive functions' tests used. The traditional executive functions' tests were used concurrently with the less common ones. Therefore, the examination of the feasibility of these non-conventional executive tests in clinical stroke population was possible. The Hayling test and Questioning task proved to differentiate stroke patients from healthy control subjects and in the future, these particular methods can be used in assessing executive functions in clinical stroke population. This is important, since measuring executive functions is difficult particularly in the elderly, and more sensitive methods are needed; even if the executive functions are vulnerable to subtle changes caused by increasing age, particularly intact executive functions are crucial for functional independence. Thus, when assessing the elderly stroke survivors, the distinction between normal age-related changes and pathological changes, potentially leading functional disability, is important. In addition, according to the correlations between established and less common tests of executive functions, it can be argued, that specifically inhibition, productivity, efficient strategy formation and switching, as well as perseveration tendency are associated with stroke patients' functional dependence. There are no previous studies documented, that have used such a wide and comprehensive executive functions test battery on prediction of basic activities of daily living and instrumental activities of daily living among stroke patients. In addition, the Hayling test, Questioning task and Design fluency task have not been previously studied with stroke patients. The present study confirms the value of the Hayling test and Questioning task in clinical assessment of executive functions. Furthermore, the present results indicate, that the performances on the Hayling test, Questioning task and Design fluency are associated with basic and more complex functional abilities in the stroke patients.

There is no golden standard for measuring executive functions, and their reliable assessment is challenging. The nature of executive functions is complex, and the concept includes several distinct subdomains. The clinical neuropsychological examination is highly structured and may not reveal deficits in complex executive functions. Based on the present study, it is crucial to use different methods for comprehensively assessing executive functions. In the future, it is necessary to increase knowledge of different domains of executive functions and their basis in the neural network for better understanding of the human cognition and even developing more efficient assessment methods. A few assessment methods are established in clinical use, i.e., the Trail Making test, Stroop test, Wisconsin card sorting test and Verbal fluency task. However, the sensitivity and specificity of these tests as measurements of executive functions is insufficient, since the successful test performance requires several cognitive abilities separate from executive functions (Lezak et al., 2012; Stuss, 2007). More methods are needed for better clinical neuropsychological evaluation. According to previous findings with different clinical populations, the Hayling test, Design fluency task and Questioning task may be potential assessment methods of executive functions (Burgess & Shallice, 1996; Jones-Gotman & Milner, 1977; Laine & Butters, 1982). However, thus far they have not been widely studied. In the present study, these non-conventional tests are also associated with stroke patients' functional abilities in daily living. This may indicate these tests have value outside the examination situation, i.e., ecological validity. In the future, confirmation for this hypothesis is important.

In summary, the results from the present study are convergent with the previous studies, where executive dysfunction effects on activities of daily living and instrumental activities of daily living (e.g. Pohjasvaara et al., 2002; Grigsby et al, 1998). The Hayling test and Questioning task and the four traditional tests of executive functions differentiated stroke patients from healthy controls. The Hayling test was most consistently associated with functional disability as evaluated with mRS and IADL three months after stroke, and it further predicted functional disability at 15 months. The present study emphasizes the importance of assessing executive functions in clinical populations, when predicting functional disability even in the long-term.

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APPENDIX 1
Instrumental Activities of Daily Living (IADL) Scale (Lawton & Brody, 1969)

1. Ability to use telephone	1 Operates telephone on own initiative; looks up and dials numbers.
	1 Dials a few well-known numbers.
	1 Answers telephone, but does not call.
	0 Does not use telephone at all.
2. Shopping	1 Takes care of all shopping needs independently.
	0 Shops independently for small purchases.
	0 Needs to be accompanied on any shopping trip.
	0 Completely unable to shop.
3. Food preparation	1 Plans, prepares and serves adequate meals independently.
	0 Prepares adequate meals if supplied with ingredients.
	0 Heaths and serves prepared meals or prepares meals, but does not maintain adequate diet.
	0 Needs to have meals prepared and served.
4. Housekeeping	1 Maintains house alone with occasion assistance (heavy work).
	1 Performs light daily tasks such as dishwashing, bed making.
	1 Performs light daily tasks, but cannot maintain acceptable level of cleanliness.
	1 Needs help with all home maintenance tasks.
	0 Does not participate in any housekeeping tasks.

5. Laundry	1 Does personal laundry completely. 1 Launders small items, rinses socks, stockings, etc. 0 All laundry must be done by others.
6. Mode of transportations	1 Travels independently on public transportation or drives own car. 1 Arranges own travel via taxi, but does not otherwise use public transportation. 1 Travels on public transportation when assisted or accompanied by another. 0 Travel limited to taxi or automobile with assistance of another. 0 Does not travel at all.
7. Responsibility of own medication	1 Is responsible for taking medications in correct dosages at correct time. 0 Takes responsibility if medication is prepared in advance in separate dosages. 0 Is not capable of dispensing own medication.
8. Ability to handle finances	1 Manages financial matters independently (budgets, writes checks, pays rent and bills, goes to bank); collects and keeps track on income. 1 Manages day-to-day purchases, but needs help with banking, major purchases, etc. 0 Incapable of handling money.

APPENDIX 2

National Institutes of Health, National institute of Neurological Disorders and Stroke. Stroke Scale (NIHSS) (Goldstein, Bertels & Davis, 1989).

Instructions	Score
1a. Level of consciousness	0 = Alert; keenly responsive.
	1 = Not alert; but arousable by minor stimulations to obey, answer, or respond.
	2 = Not alert; requires repeated stimulation to attend, or is obtunded and requires strong or painful stimulation to make movements (not stereotyped).
	3 = Responds only with reflex motor or automatic effects or totally unresponsive, flaccic and areflexic.
1b. LOC questions (the month and his/her age)	0 = Answers both questions correctly.
	1 = Answers one question correctly.
	2 = Answers neither question correctly.
1c. LOC commands (open and close eyes, grip and release the non-paretic hand)	0 = Performs both tasks correctly.
	1 = Performs one task correctly.
	2 = Performs neither task correctly.
2. Horizontal eye movements	0 = Normal.
	1 = Partial gaze palsy; gaze is abnormal in one or both eyes, but forced deviation or total gaze paresis is not present.
	2 = Forced deviation, or total gaze paresis not overcome by the oculocephalic maneuver.

3. Visual fields	0 = No visual loss. 1 = Partial hemianopia. 2 = Complete hemianopia. 3 = Bilateral hemianopia (blind including total cortical blindness).
4. Facial palsy	0 = Normal symmetrical movements. 1 = Minor paralysis (flattened nasolabial fold, asymmetry on smiling). 2 = Partial paralysis (total or near-total paralysis of lower face). 3 = Complete paralysis of one or both sides (absence of facial movement in the upper and lower face).
5. Motor arm	0 = No drift; limb holds 90 (or 45) degrees for full 10 seconds. 1 = Drift; limb holds 90 (or 45) degrees, but drifts before full 10 seconds; does not hit bed or other support. 2 = Some effort against gravity; limb cannot get maintain (if cued) 90 (or 45) degrees, drifts down to bed, but has some effort against gravity. 3 = No effort against gravity. 4 = No movement.
6. Motor leg	0 = No drift; leg holds 30-degree position for full 5 seconds. 1 = Drift; leg falls by the end of the 5-second period but does not hit the bed. 2 = Some effort against gravity; leg falls to bed by 5 seconds, but has some effort against gravity. 3 = No effort against gravity; leg falls to bed immediately. 4 = No movement.

7. Limb ataxia (the finger-nose-finger and heel-shin tests are performed on both sides)	0 = Absent. 1 = Present in one limb. 2 = Present in two limbs.
8. Sensory	0 = No sensory loss. 1 = Mild-to-moderate sensory loss; patients feels pinprick is less-sharp or is dull on the affected side; or there is a loss of superficial pain with pinprick, but patient is aware of being touched. 2 = Severe or total sensory loss; patient is not aware of being touched in the face, arm, and leg.
9. Language	0 = No aphasia; normal. 1= Mild-to-moderate aphasia; some obvious loss of fluency or facility of comprehension, without significant limitation of ideas expressed or form of expression. Reduction of speech, however, makes conversation impossible. For example, in conversation about provided materials, examiner can identify picture or naming card content from patient's response. 2 = Severe aphasia; all communication is through fragmentary expression; great need for inference, questioning, and guessing by the listener. Range of information that can be exchanged is limited; listener carriers burden of communication. Examiner cannot identify materials provided from patient's response. 3 = Mute, global aphasia; no usable speech or auditory comprehension.
10. Dysarthria	0 = Normal. 1 = Mild-to-moderate dysartria; patient slurs at least some words and, at worst, can be understood with some difficulty. 2 = Severe dysartria; patient's speech is so slurred as to be unintelligible in the absence of or out of proportion to any dysphasia, or is mute/anarthric.

11. Extinction and inattention (formerly neglect)	0 = No abnormality. 1 = Visual, tactile, auditory, spatial, or personal inattention or extinction to bilateral simultaneous stimulation in one of the sensory modalities. 2 = Profound hemi-inattention or extinction to more than one modality; does not recognize own hand or orients to only one side of space.